and asthma is not precisely known. NSAIDs have been found to routinely cross-react with ASA in these subjects.\textsuperscript{2,3} Furthermore, the degree of sensitivity to a particular NSAID appears to be directly related to the potency of that analgesic as an inhibitor of prostaglandin synthesis in vitro.\textsuperscript{4} Thus, the greater the potency of a NSAID to inhibit cyclooxygenase in vitro, the lower the dose that will be required to provoke bronchospasm and/or nasal ocular reactions in ASA-sensitive subjects with rhinosinusitis and asthma.

The original observation of Szczeklik et al\textsuperscript{4} in 1977 that drug behavior in aspirin-sensitive asthmatics could be predicted on the basis of in vitro inhibition of cyclooxygenase has been consistently reaffirmed.\textsuperscript{3,8} Whether this shared pharmacologic effect participates in the pathogenic mechanisms accounting for adverse responses to ASA/NSAIDs has never been proved. Cyclooxygenase inhibition, with simultaneous formation of arachidonate, shunts arachidonic acid metabolites through the 5-lipoxygenase pathway with formation of leukotrienes which in turn can stimulate bronchoconstriction, mucus secretion, and chemotaxis.\textsuperscript{8} Ferreri et al\textsuperscript{3,8} have demonstrated increased concentrations of LTC, in nasal secretions during ASA-induced respiratory reaction. Arm et al\textsuperscript{4} reported greater airways responsiveness to inhaled LTE, in ASA-sensitive than nonsensitive asthmatics. However, after ASA desensitization, threshold sensitivity to LTE, was markedly reduced. ASA desensitization has been shown to decrease the level of inflammation in the respiratory mucous membranes of these patients,\textsuperscript{7} presumably by inhibiting leukotriene synthesis\textsuperscript{5,6} and/or by down-regulating receptor responsiveness to these prostanooids.\textsuperscript{11}

We have demonstrated cross-reactivity between ASA and flurbiprofen in an ASA-sensitive subject with rhinosinusitis and asthma, thus reinforcing the observation that NSAIDs capable of cyclooxygenase inhibition predictably cross-react with ASA. Flurbiprofen is the newest of this class of drugs that we recognize to block cyclooxygenase. In such patients, if ASA/NSAIDs are required in the treatment of ongoing arthritis, cardiovascular disease, or the underlying rhinosinusitis/asthma, ASA/NSAID desensitization can be employed to allow continued use of these medications.\textsuperscript{12}

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Monitoring of Serum KL-6 Antigen In a Patient with Radiation Pneumonia*  
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Serum marker KL-6 antigen has been reported to be a valuable indicator of the disease activity of interstitial pneumonia.\textsuperscript{1} It is not clear how sensitive the serum KL-6 antigen level is in reflecting histologic changes in lung tissues. We report here the results of serial measurements of serum KL-6 antigen in a 76-year-old male patient with radiation pneumonia. Serum KL-6 antigen levels were more sensitive than lactate dehydrogenase and procollagen type III N-terminal peptide. The level of serum KL-6 antigen appears to reflect the histologic changes of the lung more sensitively than does C-reactive protein. (Chest 1992; 101:855-60)

CRP = C-reactive protein; LDH = lactate dehydrogenase; P3P = procollagen type III N-terminal peptide.

We have reported that a new serum marker, KL-6 antigen, is a useful indicator of disease activity in patients with interstitial pneumonia.\textsuperscript{1} However, the sensitivity of this marker in reflecting pulmonary tissue damage has not been established. We studied the time course of serum levels of KL-6 antigen in a patient with radiation pneumonia and compared it with that of other serum markers—lactate dehydrogenase (LDH), procollagen type III N-terminal peptide (P3P), and C-reactive protein (CRP)—to assess their usefulness in evaluating the activity of interstitial pneumonia.

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CASE REPORT

A 76-year-old man began to complain of cough with sputum and general fatigue two months before admission to our hospital. He had first visited a local hospital, where a chest x-ray film revealed a nodular shadow with pleural indentation in the left lung field (Fig 1, A).

On the patient's admission to our hospital, breath sounds were normal, and lymph nodes were not palpable. Histologic examination of the percutaneous lung biopsy specimen revealed the large cell type of lung cancer. The main tumor was resected, but the complete curative operation could not be carried out because the hilar lymph nodes were adherent to the pulmonary veins.

After the operation, the patient received a course of radiotherapy over the mediastinum and left supravacuicular area (1.8 Gy/d). When the patient began to complain of dysphagia ten days after the initial radiation treatment, the course was discontinued. When his clinical symptoms improved, the therapy was resumed. But fever and dyspnea increased, and a chest x-ray film revealed an infiltrative

![Clinical course.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21640/)

**FIGURE 2.** Clinical course. Cutoff levels of KL-6 antigen, P3P, and LDH were 520 U/ml, 0.8 U/ml, and 123 IU/L, respectively. The CRP level was 0.25 mg/dl. P3P = P3P.
process suggesting radiation pneumonia (Fig 1, B). In spite of the administration of a high dose of adrenocortical hormones, respiratory failure worsened. The patient died of respiratory failure 50 days after the commencement of radiotherapy.

The levels of the serum markers LDH, P3P, CRP, and KL-6 antigen, which indicate the activity of interstitial pneumonia, are shown in Figure 2. The level of CRP was increased gradually to 22.8 mg/dl, but no more elevation was observed afterward. The LDH level was abnormally high just two days before the patient's death. The P3P level was abnormally high during radiotherapy, but the level temporarily decreased and then became elevated again two days before the patient died. In contrast, the KL-6 antigen level rose to 810 U/ml when the patient complained of dysphagia, but decreased into the normal range when radiotherapy was discontinued. However, the KL-6 level was increased again at the time when radiation pneumonia was diagnosed and rose remarkably to 16,640 U/ml two days before the patient's death.

Histologic examination of the autopsy specimens of the lung revealed the presence of hyaline membranes, regenerating type II pneumocytes, and fibrotic changes in the interstitium. Immunohistologic study of the lung sections showed that KL-6 antibody reacted with regenerating type II pneumocytes and macrophages or type II pneumocytes in air spaces but did not react with interstitial components (Fig 1, C), as we reported previously.7

**DISCUSSION**

Radiation pneumonia is one of the factors that restrict the use of radiotherapy against lung cancer. There are only a few methods for diagnosing and assessing the disease activity of radiation pneumonia—chest radiography, 67Ga citrate scintigraphy, 68Ga citrate scintigraphy,8 spirometry, and evaluation of serum markers, such as LDH and P3P.4

DeRemee2 first reported the use of LDH as an indicator of the presence and disease activity of interstitial pneumonia. The peptide released during the conversion of type III procollagen to type III collagen, P3P, is a potential marker of fibroblast activity. Serum P3P has been reported as a marker of disease activity of interstitial pneumonia,9 particularly of radiation pneumonia.

The monoclonal antibody that we developed, KL-6, recognizes a carbohydrate antigen expressed on type II pneumocytes.6 Soluble KL-6 antigen is a circulating mucin-like glycoprotein, which can be detected by sandwich assay using the monoclonal antibody KL-6. This antigen has been identified as a potential indicator of the extent of the disease activity of interstitial pneumonia.1 The findings in this patient suggest that serum KL-6 antigen may be a more sensitive marker of radiation pneumonia than LDH or P3P and may reflect the histologic changes of the disease more sensitively than CRP does.

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**Pulmonary Toxicity following Exposure to Methylene Chloride and its Combustion Product, Phosgene**

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Chemical paint removers containing methylene chloride are widely used in domestic and industrial settings where exposure to a heat source with conversion to phosgene is possible. We describe a case of noncardiogenic pulmonary edema and subsequent hyperreactive airways following such an exposure. In addition, the various problems that have been associated with exposure to methylene chloride and phosgene are reviewed. (Chest 1992; 101:860-61)

**MC = methylene chloride**

Methylene chloride, CH₂Cl₂ (MC), or dichloromethane, is a common ingredient of many paint removers that are employed by individuals renovating older homes or repairing furniture. While warnings to use this substance in well-ventilated areas are common, they are often used in poorly ventilated areas and may be exposed to a heat source to facilitate paint removal. The industrial and domestic use of MC is equally widespread. The authors would like to stress the need to better inform individuals exposed to this substance concerning the risks of MC inhalation, the risk of phosgene production when exposed to a heat source, and the need to ensure adequate ventilation during its use.

**CASE REPORT**

A 34-year-old man presented to the Emergency Department with complaints of dyspnea and vague discomfort in the midchest region. Medical history was unremarkable. The patient had been using a nationally advertised brand of paint remover, consisting of MC (>80 percent by weight) as well as small amounts of methanol propoxyl and ethylene glycol monobutyl ether, while refinishing the woodwork in a 180 x 360-cm foyer without windows. The patient applied the product with a paint brush and then scraped it off with the aid of an electric hot air gun. After working for 8 h and using 504 g of the product, he developed headache, cough, and chest discomfort. These symptoms persisted despite leaving his home, so he came to the Emergency Department for further evaluation.

At that time the vital signs were stable, and the chest roentgen-